

COLLINS (Jos)

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ACROMEGALY.



• BY •

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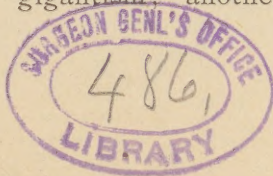
ACROMEGALY.

By JOSEPH COLLINS, M.D.,

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The disease now known to the profession as acromegaly is of comparatively recent date, it being scarcely six years since it was first accurately described as it showed itself in two of Charcot's patients, both females, at the Salpêtrière. It is unnecessary to say that homage is due to P. Marie for first describing the disease with precision; indeed, Verstraten has given to it the name of Marie's disease, and many writers following him have referred to it in the same way. However much we may deprecate the application of personal names to particular diseases, it would probably be advisable to continue designating the symptom complex known as acromegaly, as Marie's disease, until we have learned something about its causation and pathology, and then give to it a name based on such acquired knowledge, particularly the latter. The term acromegaly is especially inappropriate, its literal meaning being simply large extremities. In the disease to which the name is applied, however, the changes in the face are as of much importance and as frequent occurrence as in the extremities. Therefore the clinical picture called up by the term acromegaly does not literally suggest the disease described by Marie. Mosler, in an extensive critical study of the disease, and particularly of the arguments put forth by Souza-Leite in his well-known monograph, argues that we should refer to the disease as pachyacia, a word which would in a way signify that the change was a thickening of all the structures of a part involved, and this not alone of the extremities. Recklinghausen was the first to put forward this term pachyacia, and Mosler concurs in its propriety.

Like a great many other diseases that are seemingly of recent date, acromegaly has probably been noticed and described under other names for many decades past. A disease which was probably acromegaly was reported as seen in two cases by Friedreich, under the title of "hyperostosis of the entire skeleton;" another by Fritsche and Klebs, under the title of "gigantism;" another by



Lambroso as "general hypertrophy, macrosomia." Then no doubt some of the cases that have come to light under the heading of myxoedema have been of this nature, particularly a case by Henrot reported under this title. Souza-Leite thinks that there can be no question but that a case by Saucerotte-Noel in 1772 was really a typical case of this disease. A critical search of the literature of the past century would be likely to yield other cases which were quite as characteristic as those reported by Marie. This does not in the least detract from the honor due Marie for calling the attention of the profession to this pathological entity in such a lucid and explicit way, that although a great number of cases have since been reported, no additional important symptoms have been produced.

In Souza-Leite's brochure, which is a most complete exposition of the subject up to the date of its appearance, a complete record of all the published cases are to be found. More recently a translation of Souza-Leite's article under the auspices of the New Sydenham Society has appended to it the notes of nine cases, the reports of which had appeared in the journals between the time of the appearance of the brochure and its translation. This brought the sum total of cases up to forty-eight, which probably includes every case on record till near January, 1891. The principal object of this present digest is to bring the bibliography of acromegaly up to date, and to note and discuss any advances that have been made in respect to the disease, either in its etiology or pathology. It is a deserved compliment to Marie to say, that so thorough and critical was his description of the disease as originally observed by him, that really nothing of importance has been added to the symptomatology of the disease since that time. Although the clinical picture presented by acromegaly is very well known, it will probably be of no disadvantage if we take a glance at the history and development of the disease before we present the notes of the cases that have been recently published.

As regards the etiology of the disease it may be said that it occurs somewhat more often in males than in females. Although we cannot speak definitely concerning its appearance in the different races, racial differences probably offers no exemption. A case has recently been described in a negro (Berkley). Although it may appear at any age, the larger proportion of cases by far

first show themselves between puberty and early adolescence (19 to 26, Souza-Leite). It may show itself at a very early age (Rolletson's case), or it may first present itself long after middle age (Erb's, Waldo's, and Hare's cases). Congenital and hereditary influences are excluded from etiological significance in this disease by Marie. He is particularly decided on the point that those cases that have been described under the heading of congenital acromegaly do not belong to the category of true acromegaly as he has described it. Recently, however, some cases have been reported that would tend to show that hereditary influences may have some place in its causation.

Among the exciting causes mentioned are fright (Pel), mental depression (Pechardre), syphilis (Marie, Brigidi, *et al*), exposure to cold (Marie, Verstraeten), traumatisms, either falls or direct injury (Minkowski), rheumatism or gout (Hadden, Ballance, Marie, Souza-Leite, Goodlee, *et al*), alcoholism (Brigidi, Osborne), the exanthematous fevers, such as variola, scarlatina, malaria, and bronchitis, epistaxis, multiple abscess, severe and prolonged cardiac palpitation, abortion, have all been mentioned by one or more writers as having preceded the appearance of the symptoms of acromegaly, but their connection would not seem to be a very intimate one. In most of the cases published within the last two years there has been absolutely no apparent connection between an etiological influence and the appearance of the disease. In some few cases (Hare, Rolletson, Litt-hauer), the extremities had been large so long as the patient could remember.

The theories that have been forwarded concerning the actual causation of the disease may be stated as follows:

1. Marie's. That the disease is a systematic dystrophy dependent in some obscure way upon the disease of an organ, the pituitary body, the functions of which are as yet unknown. It is only just to say that although a comparatively large number of autopsies have shown that there was a lesion in the hypophysis cerebri in many of the cases, Marie does not support this theory with any more vigor than formerly; that is, he is still inclined to believe that the pathogeny of the disease is yet to be demonstrated. A considerable number of cases yet under observation, of which may be mentioned Osborne's, Bignami's, Bard's, Hare's, present symptoms

that are apparently dependent on and traceable to a lesion in the pituitary body.

2. Klebs'. This pathologist, astonished by the existence of the thymus in his case, and taking into consideration a symptom known as post-sternal dullness which had some importance attributed to it by Erb, formulated the theory that the thymus persisting was the seat of vascular budding and proliferation, angioblasts were produced and these formed the foci of the change that went on in the affected parts of the body.

There are serious objections to this theory, the prominent one being that in many cases it is found on post-mortem that the thymus has not persisted; indeed Klebs had a case sometime after formulating the above hypothesis in which there was no post-sternal dullness. Then again there are other conditions attended with persistence, or even hypertrophy of the thymus, and which are not associated with the development of acromegaly. It must also be remembered that it was not possible to prove that the thymus was the middle point of the vascular budding.

3. Virchow's. This pathologist thinks that in acromegaly we have only half a disease described, *i. e.*, the latter half, with its degenerative details, while at an earlier period it is often accompanied by an increase of muscular power, and is in some instances apparently hereditary. Freund's case lends considerable support to this view.

4. The nervous theory. In spite of the fact that it is based on no positive knowledge, the theory that acromegaly is a nervous disease has taken a very firm hold on the minds of those who have seen most of the disease.

A favorite supposition of physiologists is that there is no organ in the body in post-uterine life but what has some physiological function to perform. This was the principal reason why Klebs' theory was not greeted with any enthusiasm; the thymus is a body which plays no part in post-uterine life. On the other hand, the pituitary body is always present, and the supposition is that it is a glandular body, particularly the pre-hypophysis. The histological structure of this part of the pituitary gland, being made up of convoluted tubules lined with epithelium and highly vascular as it is and its origin, favors this view. Ragowitsch reasoning from the results obtained by Marmesco by removing the hypophysis in some rabbits, is inclined to favor the view that these

glands secrete a substance the retention of which in the system, and particularly its action on the nervous system, facilitates the development of acromegaly. If this theory gain acceptance, as pure theory, it would be easy to follow out a process of reasoning such as is suggested by Marie and Marmesco in the "*Archives de méd. et d'anatom. path.*" for July, 1891, and say that the accumulation of this poison in the extremities and face from some special predilection brings about a condition which is the equivalent of the hyperæmia of inflammation and which is followed by the hypertrophic changes so apparent in the disease. If this theory could be in any way proven, the disease would then take its place as one of the auto-toxæmic diseases.

The symptoms of the disease present themselves very gradually and are preceded or not by perversions of the sexual functions (amenorrhœa in women, sexual weakness in man). The first thing noticed is a gradual enlargement of the fingers and hands, and simultaneously, or a little later, the feet are involved. The enlargement affects the soft parts as well as the hard, and goes on to an enormous extent. The fingers become sausage shape; the hands, principally because of the great increase at the wrists, battledore shape. The arms are rarely affected. Except in some cases a widening of the epiphysis at the elbows and atrophy of the muscles. The fingers appear short; the nails, though greatly increased in size, do not generally present any trophic trouble, and there is no deformity of the extremities. In the feet the large toe may become increased out of all proportion to the rest of the foot. The changes in the head are principally confined to the upper and lower jaw, particularly the latter, which gives the prognathous face. The thing that may first attract the patient's notice, however, is that each time that he purchases a new hat it must be a size larger (Osborne). The nose, lips, especially the lower, and the tongue are enormously enlarged. The alveolar processes are frequently widened and the teeth separated. The eyelids become elongated, the lashes coarse and unwieldy, and the color of the lids a mild brown. The shoulder girdle is enlarged principally from the participation of the clavicle in the hypertrophy. Occasionally there is an area of post-sternal dullness at the upper part (Erb). The trunk presents two curvatures, a more or less marked kyphosis in the cervico-dorsal region, and an

anterior deformity due to involvement of the lower portion of the thoracic cage. The deformity has been aptly compared by Marie to the figure of Punch. There is frequently a slight degree of scoliosis, and always, if the course of the disease is sufficiently long, a compensating lordosis in the inferior dorsal and upper lumbar region. The pelvis is frequently involved, but only to a moderate extent. Ordinarily there is no disturbance of sensation. The hearing is frequently affected and the ears are greatly enlarged. There is often a considerable degree of exophthalmos, and occasionally unilateral hemianopsia and homonymous hemianopsia. The optic disc is occasionally very pale and the veins of the retina turgid. The larynx is frequently augmented in volume not alone in man, but in woman, and the voice becomes more grave, stronger, of longer duration, and especially disagreeable. The speech is slow, embarrassed, guttural, and seems to stick in the mouth. The face takes on the appearance of an elongated oval, and the sexual organs are frequently atrophied. The disease may be preceded in its appearance by any variety of hybrid symptoms, having more or less intimate relation to the disease. They are headache, malaise, mental apathy, varying pains, feelings of premonition, change in temperament, bodily weakness and loss of ambition, markedly increased appetite, great somnolence (Packard), perversion of *morale*, a dry skin, which has a tendency to crack, and polyuria. Many of these symptoms may attend during the course of the disease.

The symptoms have been elaborately classified by Souza-Leite as follows:

1. Objective.
2. Subjective.
3. General.

Each of these two first groups may be subdivided into:

- (a) Constant, fundamental, or principal symptoms.
- (b) Inconstant, accessory, or secondary.

This classification will be found very useful even though it be somewhat artificial; but it is not possible to here enter into a consideration of it.

The following cases have appeared since the English translation of Souza-Leite's brochure, and will, with the list appended to the end of this paper, I hope, bring the bibliography of the disease up to date. It will be remembered that the number of cases in that translation was

brought up to forty-eight. The following cases will be numbered from that number onwards, without respect to priority of publication.

OBSERVATION XLIX.—(Stembo.) Woman, aged forty, who first presented symptoms of the disease concomitantly with the appearance of the climatic at the age of thirty. She first noticed enlargement of the feet and hands so that her shoes and gloves would not fit. The enlargement was after noticed in the nose, the lower jaw, lower lip, and the tongue enormously; likewise the palate and a part of the larynx. The ears remained normal; voice deep and masculine; urine increased in quantity, no sugar or albumen, no disturbance of sensation. Right patellar reflex absent; left, weak; internal organs, normal. No apparent causation for the development of the disease.

OBSERVATION L.—(Litthauer.) Male; good family and personal history; married; three children, two died in infancy. Disease first showed itself thirteen years before. The hands and feet began to enlarge, and went on increasing for two years and then stopped. In the beginning the hands did not give him any particular trouble, but now they often become "sleepy," and he cannot do his work. Formerly his sexual appetite was enormous and was gratified; now the sexual functions are normal. He denies syphilitic infection. Mucous membranes pale; no œdema; no eruption on the skin; no sensory disturbances. Some kyphoses; ideation slow; speech altered; mental hebetude. Pupils normal. Perverted proportion between the size of face and head. Face has assumed an oval shape mainly from increase in size of the lower jaw. Nose, greatly enlarged; the lower lip likewise and somewhat cyanosed. Neck short and thick, circumference 41 c.m. No post-sternal dullness. Heart and lungs normal. Urine and genital apparatus normal. Red and white blood corpuscles normal in proportion. Hæmaglobin remarkably decreased, 40 per cent. Hands cold to the touch, battledore shape; fingers, sausage shape. Marked anæmia. Myopia of both eyes; field of vision limited; retina normal. No disturbance in sensation or electrical reactions.

OBSERVATION LI.—(Pel.) A girl, previously healthy, of good family history, and with no acquired neuropathic predisposition, received just at the time of menstruation a severe psychical trauma. From this time she dates all the symptoms of the present trouble. First she had gen-

eral nervous symptoms, such as head and body ache, paræsthesia, psychical depression, apathy, etc. Soon after this the hands, feet, and face began to enlarge. In due time a complete picture of acromegaly was developed. She has had amenorrhœa since the time of the fright, although the genital apparatus seems normal. No post-sternal dullness or other evidence of persistent thymus. Thyroid apparently smaller. Author gives it as his opinion that the trouble is neurotic.

OBSERVATION LII. (Bignani.) Female, forty-nine years old. Symptoms began when twenty-five years old, and came on after an abortion which was accompanied by a great loss of blood. Since that time she has not menstruated. There are no hereditary or etiological factors with the exception of the abortion. At the beginning of the disease there were vague pains, paræsthesia, pains in the bones and joints, headache, and then the remarkable increase in size, which was participated in by the lower jaw, the skull, scapulæ, clavicles, larynx, and extremities. Muscular power began gradually to decrease; moderate degree of exophthalmos on both sides; ophthalmoscope showed simple atrophy of the papillæ, right external strabismus, nystagmus, limitation of the movability of the eyeballs in all directions; appetite enormously increased; general muscular weakness without apparent muscular atrophy; skin thickened in places, and, with the exception of slight sensorial disturbances in the hands, sensibility was intact; weakness of the patellar reflexes; cardia hypertrophy; sensation of taste rather slow in its response. The disease made far greater progress in the first part of its course than the last.

OBSERVATION LIII. (Graham.) Male, aged thirty-nine; presented the following marked features: Enlargement of the face; thickness of the lips, especially the lower one; face elliptical in shape; hypertrophy of superior and inferior maxillæ; atrophy of the optic nerves; enlargement and flatness of the hands, feet likewise enlarged; arms and legs normal in size. The disease had lasted for upward of five years.

OBSERVATION LIV.—(Graham.) Male, died aged fifty-one. The disease commenced when he was about twenty-five years of age. He presented the following conditions: Enlargement of the head and face; prominent eyebrows; nose enlarged; hypertrophied superior and inferior maxillæ; lips thickened, especially the lower one; face elliptical in shape and enlarged in every way, resting upon the upper

and anterior portion of the chest; neck short and thick; marked kyphosis of the spine in the upper dorsal and lower cervical vertebræ sternum very prominent; enlargement of the scapulæ, scoliosis, lumbar lordosis. Hands were enormously enlarged, as were also the feet. No marked change in the arms or legs with the exception of the knees which were increased in size. No post-mortem examination was made.

In both these cases the soft parts and bones were enlarged; the vitality diminished; the mental faculties impaired; the voice was altered in both, and there was sexual weakness, but children were begat in both cases after the disease had shown itself.

OBSERVATION LV.—(Paget.) Male, aged forty-two; disease had been progressing for ten years. There was extreme lengthening of the face, with overgrowth of the facial bones, particularly of the inferior maxillary. The hands and feet were enormously and characteristically enlarged. The patient had lost six inches in height from the advancing deformity of the spine. Thyroid apparently enlarged, vision defective, molluscous growths on the trunk, and osteophytes in the knee-joint. Voice thick and guttural. Loss of muscular strength.

OBSERVATION LVI.—(Bury.) The author presented to the London Pathological Society the brain and thyroid of the patient who was the subject of the following sketch: Female, twenty-three years of age, who had been troubled with loss of strength and headache for upward of three years. Eighteen months before death her sight began to fail. She presented great prominence of the orbital arches, low retreating forehead, enlargement of the nose, lips, tongue and body of lower jaw. Voice low-pitched and monotonous, speech low-pitched and deliberate. Right lobe of thyroid gland unduly prominent. Hands, feet and digits enlarged, increased principally in their breadth and thickness. Kyphosis and slight scoliosis of the upper dorsal and lower lumbar vertebra. Abdomen enlarged and its walls thickened; limb muscles soft and flabby, but no paralysis. Reflexes normal. Taste, smell and hearing unaffected. Left eye nearly blind; temporal hemianopsia of the right eye. Sugar in the urine, and death from coma.

On autopsy, there was found a pulpy tumor at the base of the brain, excavating the sella turcica and extending from the optic chiasma, which, with the optic tracts, were compressed to the cerebellum. Microscopic-

ally, the tumor was apparently a glioma. Each lobe of the thyroid was found enlarged and contained a cyst. Pendant masses were found attached to the pericardium, similar to a persistent thymus. Heart and liver normal. Uterus small, infantile. Small cysts in ovaries. With the exception of severe headache, starting in the left temple, there had been no sensory disturbances in this case.

OBSERVATION LVII.—(Boltz.) Male, forty-one years of age, of good family history, has one boy seven years of age who has always been in good health. While the patient was at school he was troubled a great deal with attacks of cardiac palpitation, and later had an attack of pneumonia. In later years dyspepsia and hemorrhoids have been troublesome. He cannot exactly state when the present illness began. The first thing that he noticed was bodily weakness and then trouble in reading, and shortly after the defect of vision prevented him from working. He presented the ordinary typical face and countenance of acromegaly. Teeth good and held firmly in their sockets. Tongue enormous, the filiform papillæ greatly enlarged, giving rise to the so-called hairy tongue. Hair strong and coarse, beard scanty. Clavicles elongated, principally from growth at the acromial ends; muscles of shoulder girdle atrophied. Moderate kyphosis of the cervical vertebra. Tonsils normal; epiglottis enlarged and thickened; thyroid somewhat smaller, probably atrophic on the right side. Hands and finger present the characteristic enlargement. Patella and both epiphyses of the tibia enlarged. Feet enormously enlarged. Visceral organs normal, no post-sternal dullness; urine normal; muscular strength lessened; sensation and reflexes normal; intelligence not disturbed, but answers very slowly. Voice deep, and sounds if it were hindered in the throat. Sexual desire and ability has been absent for seven years, although the genital organs appear to be normal. Taste, smell, and hearing normal. Denies venereal infection. Bitemporal hemianopsia; rotatory nystagmus when he fixes sharply. To explain the bitemporal hemianopsia, we must have a lesion of the inner crossed fibres of the optic nerve in the chiasm, and an intact condition of the outer uncrossed. The writer, therefore, believes that this case is probably due to an increasing or proliferating tumor of the hypophysis cerebri which has caused an atrophy of the inner crossed fibres of chiasma, the outer uncrossed fibres remaining as yet

undisturbed. It might be stated in connection with this case that Schultze's case somewhat resembling this gave a left-sided hemianopsia.

OBSERVATION LVIII.—(Bradford.) The patient was a woman forty-three years of age, who had noticed enlargement of the hands and feet for the past ten years, and which came on without any apparent cause. Four years later she developed a kyphosis of the cervico-dorsal vertebra. The skin of the hands and feet was greatly thickened, both clavicles lengthed and enlarged at the acromial ends, and the thoracic cage enlarged mainly from increase in size of the ribs. The under lip was markedly enlarged, and face showed the type of acromegaly. Reflexes normal, great muscular weakness, and mentally very dull.

OBSERVATION LIX.—(Berkley.) A sixty-year-old negro woman, who presented herself for treatment on account of mental disturbance. No neuropathic inheritance. The excessive growth first began to be noticeable in 1889 and from October, 1890, to March, 1891, the period in which she was under the care of the reporter, no particular change had taken place except some trophic disturbances in the arms and hands. The internal organs apparently normal and the sensory and special sense organs are not appreciably affected. Patient troubled greatly with excessive perspiration which is exceedingly offensive. Patellar reflex good; absence of Romberg's symptom. Patient has a very wicked temper and is very weak mentally. Head, nose, lips and tongue, but not the ears, appear enormously enlarged. Hands present the characteristic enlargement; arms and forearms unaffected. In the lower extremities the patellæ and feet seem to be the only parts hypertrophied. Very little information could be obtained regarding sensation, as the patient was practically devoid of sense. The trophic disturbance of the forearms were of the nature of ulcers.

OBSERVATION LX.—(Hare.) Female, aged twenty-five, of good family history. Three years ago menstruation was irregular for a time and afterward absent for periods varying from three to six months. Then vision began to fail, first in the outer half of left eye and gradually proceeded across the eye till the vision was entirely lost; latterly the vision in right has markedly failed. She presented slight distention of the abdomen, general increase in size of all the members, posterior curvature of the vertebra, extending from the twelfth dorsal to the

seventh cervical vertebra. On the anterior surface of the thorax at the third interspace, half way between the nipple and the sternum, there is a considerable bulging due to increase in the length of the third and fourth ribs; no exostosis. On the left side the floating ribs are protruding. Nose enlarged and face massive. Considerable increase of the bony and connective tissue of the entire body. She gives the appearance of a large woman unequally developed. In three years she has gained sixty-five pounds. Distinct enlargement of the thyroid gland, but no associative circulatory disturbance. Suffers from a severe neuralgic pain in the right temporal and supra-orbital region, and occasionally sharp pains in the extremities. Variable pre-tibial œdema. Appetite good, urine rather scanty; loss of hearing on the right side, and chronic otitis media purulenta of right side. While under observation the patient had a hæmoptysis lasting for about a week, and this was followed by an epistaxis. Electrical examination shows a normal qualitative response in all parts tested, but somewhat altered quantitative reaction chiefly in the direction of a delay, especially in the thighs. Examination of blood showed 4,700,000 red corpuscles to the cubic millimetre and 11,000 leucocytes. Hæmaglobin percentage normal. Red corpuscles crenated and irregular in shape, many of them seeming to be poorly developed. Vision, R. $\frac{2}{100}$, L. O. Total atrophy of optic nerve of left side. Optic nerve of right eye is pale with shallow cupping, but not including entire disc. R. pupil normal in reaction. Left does not act alone, but only in harmony with right. Slight central color scotoma, most marked for green.

OBSERVATION LXI.—(Cohen.) Male, American, twenty-eight years of age, 6 feet $2\frac{1}{2}$ inches in height, weighing 238 pounds. At the age of sixteen he thinks he was as tall as he is now and weighed 180 pounds. He has never been troubled with spontaneous or intense headache, although headache may be brought on by study, occasionally he has confusion of ideas; until four years ago worked as a blacksmith and wielded a thirty-pound hammer. Appetite increased; great drowsiness; urine normal. Thickness and dumpiness of fingers characteristic; hands spade-like; skin thick and tough; nails broad and short, but not striated. Has comparatively little strength. Feet flat, enlarged, broad and clumsy. In two years' time the size of his hat-band has increased from $6\frac{3}{4}$ to $7\frac{1}{2}$ inches. Cervico-dorsal kyphosis with ten-

ency to forward thrust of the head; paunching of the abdomen. Varicose veins of the legs very prominent. Superciliary ridges prominent, frontal sinuses much enlarged. Malar bones enlarged and projecting laterally. Face presents typical lengthened ellipse of acromegaly. Ears enlarged and stand out at right angles from the head. Lips greatly thickened, lower lip overhanging nearly to the chin; tongue broad, thick, and furrowed. Chin much enlarged vertically, scapulæ enormous; sternal ends of clavicles stand out prominently like knobs. Sternum unusually long and xiphoid process apparently ossified. Thyroid cartilage enlarged. Thyroid gland not demonstrable. Some post-sternal dullness. Olecranon process apparently small and fossa of same name apparently much deepened, so that hyperextension of arm can be easily produced. Ophthalmoscopic examination negative.

OBSERVATION LXII.—(Harris.) Female, fifty-three years of age, of good family history; her own children healthy and intelligent. Until twenty years of age she was in perfect health, when she suffered from an intolerable neuralgia, which sometimes attacked the face and head and sometimes the extremities. As the time went on the interval between the attacks became less, until the pain was continuous. She suffered in this way for thirteen years. The pains then began to disappear, and simultaneously with the improvement she noticed changes in the face and extremities. This change was a slow increase in size of bones and cartilage of the bones of the face, neck, hands, and feet, and increase and thickening of the skin over these parts. Her mind gradually became enfeebled, and she was generally dull, apathetic, and easily fatigued, and passed the greater part of her time in bed. For six or eight years, it was said, she had a "goitre" on the right side of the neck, and for about the same length of time she had been unable to see objects on her left side. Chloroform-like odor from the patient; no post-sternal dullness; voice coarse; speech slow, thick, and often hesitating. Prominent frontal eminences; nose drawn strongly to right and enormously increased; mouth large; lips thickened; skin dirty yellowish color, and seemed slightly thickened; no obvious enlargement of malar or superior maxillary bones; great length and hypertrophy of inferior maxillary bone, and alveoli project far in front of inferior maxilla; tongue filled entire cavity of mouth; teeth lost; thyroid on right side en-

larged, on left side could not be felt; hands and feet characteristic enlargement; menstruation normal; anterior curvature of spine in upper dorsal region. Measurements made after death given in detail.

OBSERVATION LXIII.—(Holsti.) Male, who, although his parents were healthy, inherited a distinct psychical taint, and one of his brothers had some mental trouble. As a child he was sickly and weak, and, among other things, had an attack of chorea. When fifteen years old he began to grow very rapidly, and somewhat later had an attack of transient œdema of the fingers. When thirty-nine years of age he suffered an attack of typhoid fever, after which he never completely recovered his former health. Had acute pains in arms and legs very frequently. A year later he noticed that his hands and feet were growing larger, the lower jaw and chin more prominent, and his hat too small. Five years later, shortness of breath, great muscular weakness, atrophy of the muscles, especially the glutei, and could walk only with a stick; kyphosis of upper part of spine and chin brought forward toward sternum; face the shape of elongated oval, eyelids œdematous, skin light yellow color, insomnia, mind clear, hearing normal, rumbling and swashing sounds in ears, hyperidrosis, absence of pain; thyroid not to be felt, acromial ends of clavicles enlarged, cardiac hypertrophy, mitral insufficiency and obstruction. Excepting the atrophy of the thenar and hypothenar muscles, the hands and fingers are characteristic of acromegaly; legs below knee large, and feet enormously enlarged. Died of erysipelas after frost-bite.

Autopsy.—Cranium greatly thickened; brain large, 1,870 grms., with pons, cerebellum, and medulla, which weighed 240 grms.; cranial nerves appear very broad; hypophysis cerebri greatly enlarged, measuring anteroposteriorly 25 mm., side to side 30 mm., pulpy consistency. In place formerly occupied by thymus, a large, united, gray red mass, looked like whitish fat with innumerable small round bodies in it; thyroid enlarged, consistency hard; heart, liver, and spleen diseased; periosteum thickened, more adherent, especially at epiphysis; around the joints especially, surface of bone showed elevations and depressions; marked difference between epiphyses and diaphyses, former broadened and thickened, the latter appear narrow; microscopically, condensing osteitis at periphery and marked rarefying osteitis in cancelous structure; Haversian canals and lacunæ

very markedly enlarged; hyperplasia of the interstitial tissue of thyroid and general degeneration of the parenchymatous portion; the body occupying location of thymus showed fat ground substance, uncommonly rich development of blood-vessels, and some normal thymus tissue.

OBSERVATION LXIV.—(Dulles.) Male, Syrian, twenty-seven years old, of good family and personal history. Falsely charged with misdemeanor while visiting his native country and placed in prison. After liberation he was under great distrust and mental anxiety until he left the country. While in prison, hands and feet began to enlarge; had profuse sweats, great drowsiness after meals, increased appetite; has broad leonine countenance, wide malar eminences, large mouth, broad lower jaw, large chin, thick lips, lateral projections of rami of jaws. Hands and feet have characteristic enlargement. The feet have a large fleshy pad along outside and under os calcis. Internal organs and urine normal. Eyes compound myopic astigmatism, absence of hemiopic pupillary reaction; typical left lateral hemianopsia with great contraction of preserved field of vision. No improvement while under treatment.

OBSERVATION LXV.—(Fratrich.) Male patient, thirty-nine years of age. His father had epilepsy at sixty, and an uncle was likewise psychopathic. The father was short in stature and had large hands, like the patient. One brother died of meningitis and one of intestinal trouble. Patient had attack of some sickness when he was six years old, in which he was unconscious for three weeks. Until eighteen years old he was quite healthy, when the symptoms that still persist first showed themselves. He first had severe neuralgia in the forehead and pain and formication in hands and feet; great hunger, but no thirst; marked enlargement of fingers, toes, clavicles, and lower jaw; no enlargement of thyroid gland; lately general weakness and pains, beginning at the hips and going down to the tibia; right side of face more developed than left; eye normal, teeth intact, hearing normal, ears enlarged; speech slow and dragging; larynx increased and vocal cords thickened; muscles of upper extremity atrophic; condyles of radius and ulna greatly developed; hands and feet markedly enlarged; pelvis and genitals normal; sexual ability diminished; heart hypertrophied. Measurements given in detail.

OBSERVATION LXVI.—(Redmond.) Female, aged nine-

teen; admitted complaining of great weakness and swelling of hands and feet, and in wrists, knees, and ankles when she moves, and pain at night in back, right shoulder and right side. Had pneumonia three years previously, and after this remained weak, languid, constipated, and had irregular scanty menstruation. Present illness began seven months before entrance to hospital, with swelling of hands and feet, somewhat sore to the touch. She went to bed, and swelling disappeared, but hands remained enlarged. Later the knees became swollen, stiff, and painful. The present enlargement of the hands reached its extent in a few weeks. She is anæmic; fingers greatly enlarged, ends bulbous, nails slightly convex; marked increase in carpal ends of radius and ulna; back of hands considerably swollen, does not pit on pressure; knees greatly enlarged; considerable effusion into the joints; some enlargement of the heads of the tibia and fibula; patella freely movable; legs uniformly enlarged; ankles widened; effusion in ankle joints; feet wider than normal; toes thickened and bulbous, and some œdema on the back of foot; thyroid gland not to be felt; urine normal; nausea; headache; elevation of temperature; diarrhœa; melæna; inanition, etc.

[I can see no reason for calling this case one of acromegaly from the description given by the author in the original article, and it is put under this title under protest.—J. C.]

OBSERVATION LXVII. (Packard.) Male, aged forty-five; of good family and personal history. Has always had large hands and feet, and at fifteen had reached his mature growth. When thirty-seven years old he had pains all through his body, supposed to be rheumatic attack, which was followed by a very-exhaustive diarrhœa. On account of the weakness and occasional vague pains, he has been unable to work since that time. He has had three attacks of somnolence, the first lasting for three weeks, the other two lasting for a long time. His brain power had failed for several years, and he is apathetic and irritable; speech slow and deliberate, and slowness of mental response. Later on unconsciousness would appear, and remain for days at a time; before and after these attacks the somnolence would be very intense. Examination of the eyes at this time showed partial optic atrophy on both sides, with hemianopsia, both temporal fields being lost. When seen, seven years afterward, he gave a history of having suffered from severe generalized headache, with appar-

ently causeless exacerbations. The spells of somnolence have disappeared; sweats a great deal, especially in warm weather; hearing, taste, and smell are all normal; sexual desire and power absent, as it has been for fifteen years; face large and heavy, and gives evidence that it has increased in size since seven years before, when he was first under observation; the thyroid cannot be felt; no post-sternal dullness; scapulæ prominent; forward curvature of upper portion of spinal column; some lumbar lardosis and prominence of abdomen and lower portion of thorax; hands and feet markedly enlarged, but no deformity, and temperature; pain and tactile sense preserved; skin of hands soft and pliable and entirely hairless; the great toes are especially enlarged; urine albuminous. In past few years his visual field has enlarged considerably, though he still has bitemporal hemianopsia.

OBSERVATION LXVIII.—(Osborne.) Male, forty-two years old, German; has lived here for eleven years. Mother died of ascending paralysis; otherwise family history is good. Although the patient's wife is healthy, their offspring have all died of tuberculosis or croup. Patient suffered from severe attacks of epistaxis for several years when a young man; then for a period of fourteen years, although his health was not seriously impaired, he noticed continuous gradual enlargement of hands, feet, face, and body, occasional headache (often severe), vertigo, pains in bones and joints, ravenous appetite and dyspepsia, tinnitus aurium, which, with the headache, has increased to almost unbearable severity. He has had suicidal and homicidal tendencies, and always at night. He has attacks of sharp pain and a peculiar pressure feeling in the top of the head just over the region of the anterior fontanelle, which is painful on pressure, and a feeling of "rolling shot" starting from the top of his head and coursing down through his body to the feet. The headache for the past four years has ceased to be continuous, but the tinnitus aurium has continued to grow worse, as has the vertigo. With the exception of fullness of the retinal vessels, the eyes are normal. The right ear is larger than the left; the canals are increased in size; the drum is very concave, and the hammer is markedly drawn up. The right side of the whole body is more enlarged than the left. The abnormal bone and tissue growth began when the patient was about twenty years old. The hands and feet are now characteristic as described by Marie. The cranium does not seem much

altered, but the face is elongated, brow low, supra-orbital ridges very prominent, and some exophthalmos; nose very much enlarged and flattened; lower jaw projecting; lower lip and tongue markedly hypertrophied; scoliosis and kyphosis of upper dorsal region; thyroid apparently normal; larynx enlarged; voice deep, heavy, and loud; slow mentation and forgetfulness; sensation of heat and cold normal; right patella reflex absent, left very much diminished; knee-joints enlarged, and the seat of great joint pain, the finger-joints suffering also frequently; no post-sternal dullness. Since this case was reported, the upper part of the left external ear has become as hard as bone, and the right ear shows a beginning change in the same direction. The prognathism has markedly increased, and there has been considerable development of molluscum growths.

OBSERVATION LXIX.—(Denti.) Male, aged thirty-two; free from hereditary or acquired taint. The disease first made its appearance at the age of twenty-three, during convalescence from a grave attack of typhoid fever. He first noticed progressive enlargement of the hands and feet, and of the cephalic extremity, especially the face, with an increase in the height of the patient. No functional disturbance. This condition persisted for seven years, during which time the patient, a cavalry officer, was distinguished for his extraordinary robustness, uncommon muscular strength, voracious appetite, and excesses in smoking and drinking. At the end of this period the lower jaw began to increase enormously in size, likewise the hands and feet enlarged greatly, and shortly afterward the clinical picture changed. There was a breaking down of health, emaciation, loss of color, paleness of the mucous membranes, earthy pallor, great anorexia, grave and continuous lethargy, somnolency, profuse perspiration, dimness of vision first in the right eye and then in the left, then temporal hemianopsia first of the right and then of the left, and after a short period complete bitemporal hemianopsia.

The ophthalmoscope showed a congestion as of neuro-retinitis, which was followed by a bleaching of the papillary disc on the right side and then on the left. The atrophy had a neuritic character.

At this period a sort of remission in the course of the disease appeared, though the disease was not arrested. The appetite improved as did the nutrition and muscular strength, and the lethargy and profuse perspiration were

not so troublesome. Treatment: arseniate of iron, hypodermatic injections of strychnia, and the application of the galvanic current to the eye by means of the electric water bath.

OBSERVATION LXX.—(Sarbo.) Fireman, aged forty-three. On account of mental condition of patient no history could be obtained. Evidences of syphilis were present. Hands and feet were enormously enlarged, as were also the ears. Malar bones thickened, face appeared broad. The fingers were characteristic in their shape and some œdema was found in the calf of the left leg. Patient died after having been for a short time in the hospital. Autopsy showed marked thickening of the skull, especially in the frontal region; evidences in the brain of peri-encephalitis chronica, hypophysis cerebri normal, heart enlarged as was likewise the spleen, scar on glans penis, evidences of phthisical processes in the lungs. The result of the examination of the bones showed that the clavicle, the occipital bone, and the bones of the hands and feet were greatly hypertrophied and that the enlargement was not alone in the bones, but in the soft parts as well.

It is to be remarked that the kyphosis so commonly attending this disease was absent in this case. Thyroid gland apparently normal. Ends of the bones showed a condensing osteitis. (A table of measurement appended to the original.)

OBSERVATION LXXI.—(Gonzalez Cepeda.) Male, aged forty-eight; office-clerk; sanguine temperament; robust constitution. Had suffered for a long time from intense cephalalgia, which was increased in intensity by the recumbent posture. This, with weakness, had for a long time incapacitated him for work. On examination the cranium did not seem to be noticeably enlarged, the sutures were somewhat prominent. The lengthening of the face and the enormous orbital eminences were quite characteristic. The cheek bones were projecting, the superciliary ridges enlarged, and the pre-orbital circle was very prominent. The eyelids were stretched and drawn, puffed and of a dark color, the nares enlarged, the alæ swollen, and the walls of the nose greatly increased in thickness. Lips thick and fleshy, especially the lower. Lower jaw very prominent, conspicuous prognathism, jaws separated, tongue massively enlarged, so that it could be hardly contained in the cavity of the mouth. Head constantly inclined forward. Hands a

third broader and thicker than normal. Feet greatly enlarged. Judging from the history of the patient there was in the beginning some polyuria, and a great diminution of the venereal appetite, which last still persisted. Urine contained a slight and somewhat variable amount of sugar. Patient died in syncope. The autopsy showed a hypertrophic condition of the pituitary gland without any evidences of inflammation or degeneration. The increase in the size of bones was most characteristic in those of the hands and the feet; that is to say, osseous hypertrophy presented itself in the bones of the extremities and in the extremities of the bones.

OBSERVATION LXXII.—(Massalonggo.) Male, aged fifty-one; nothing hereditary in his history, and he likewise denied specific. Had always been healthy and robust, and supported without fatigue the hardships of a military life during the time of war. Without any apparent cause the symptoms of the disease began to manifest themselves in his twenty-seventh year. The symptoms then were severe pains in the left side and later in the right half of the head; he had also less frequent but more severe pain in the lumbar region and along the side of the left leg. After each attack of cephalalgia the patient would be worn out and incapable of enduring any fatigue. Two years later the patient noticed his neck becoming increased in size, and the size of his hats had to be constantly increased. At this period virile power became completely lost. It is important to mention that when the patient was about twenty-two years of age he had an attack of sickness attended with loss of consciousness and delirium which lasted for forty days, and which was called by the physicians cerebral fever. With the progress of the disease there was no cessation in the cephalalgia, lumbar pains, etc., the general debility became more marked, and the hands, feet, and head progressively enlarged. The face assumed a new outline, that of an elongated oval. Presently there appeared an extraordinary weakness of the legs, which necessitated his occupying continually a recumbent posture. Patient complained of a sense of oppression, constriction in the throat, and tachycardia. Great prominence of the superciliary ridges, frontal sinuses, the zygoma, nose, mouth, tongue, and lips. Lower jaw remarkably enlarged, and teeth of the lower jaw separated from each other for about a half centimetre. Examination of the head shows coarse gray hair, spiky osseous protuberances along the sutures, especially

the lambdoid. Thyroid is hypertrophied more in the left lobe than in the right. Cervico-dorsal kyphosis. Clavicle enlarged, sternum lengthened, thorax protuberant, sides depressed, heart hypertrophied, abdomen bulky and pendant, skin pigmented in portions, and various localities are found mollusci penduli. Sensibility normal, reflexes weak, slight paleness in fundus of the right eye, field of vision normal, timbre of voice normal.

OBSERVATION LXXIII.—(Barclay and Simmers.) Male, aged forty; Scotch, and by occupation a farmer; family history excellent. The disease began when he was twenty-five years of age. He ascribes it to a fall from a horse, and shows a depression in the skull, at the upper border of the occipital bone, about two inches in diameter, the result of this injury. At first there was violent and frequent attacks of epistaxis, and for a period of four or five years he suffered greatly from headache, which became after that period gradually less and infrequent. Joint pains were occasionally troublesome. Patient stands six feet two inches in height, and weighs twenty stones. Has great strength for a single effort, but becomes easily fatigued and is readily prostrated. Hands enormously enlarged, both the bones and the soft parts participating equally, the increase in size is chiefly lateral. Nails longitudinally striated with incurved edges; they are twice as broad as they are long. Great hypothenar masses of flesh. Wrists enlarged and bones of arm and forearm somewhat hypertrophied. Feet and legs exactly analogous to that of hands and forearm, only the hypertrophy is not so great. The tendo-Achillis is enlarged and rope-like and attached to an enormous os calcis. Nose, supra-orbital ridges, lips, and tongue greatly enlarged. Face markedly prognathus. Zygoma and malar bones prominent; antrum of Highmore apparently enlarged. Cranial bones not greatly affected. Scalp thickened and easily movable. Beard scant, hair thick, coarse and abundant. Cervico-dorsal kyphosis and compensatory dorso-lumbar lordosis; no scoliosis. Sternum greatly hypertrophied; circumference of chest at nipple 49 inches. All the joints are somewhat enlarged and give a kind of crackling noise. Thyroid cannot be felt; no retro-sternal dullness; sexual appetite in abeyance; skin pigmented in parts; knee-jerks lessened; appetite enormous; great thirst, and urine is excessive, but otherwise apparently normal. There is continuous tinnitus aurium, but no headache. He has had two or three epileptiform syncopeal attacks. Hearing and sight fairly good.

OBSERVATION LXXIV.—(Brown.) Male, aged forty-two; clergyman. Father died of anæmia at an advanced age; an uncle died of phthisis; mother epileptic. Patient had an attack of rheumatism at nine years of age, which left a mitral diastolic murmur. Has had right frontal headache for the past ten years, made worse by mental exercise, and for the past six months has suffered from palpitation; profuse acid sweats, thirst and weakness. Hands and feet were noticed to be very large while he was still young, but they have greatly increased in size during the past few years, until now they are quite characteristic in shape. Pulse 110 to 130. The face shows the typical shape of Marie. Left side is somewhat larger than the right. Thorax enlarged and a considerable number of molluscum fibrosum over neck, chest and arms. Appetite increased, urine normal. Pharyngeal linings lie in folds; voice altered. Patient seemed to improve under antipyrine and arsenic.

OBSERVATION LXXV.—(Orsi.) Female, forty-five; married, no children. Mother died of pulmonary trouble; family history otherwise good. Had intermittent fever when thirteen years old and later an attack of epidemic parotitis. Menstruated at seventeen years of age, scanty and irregular for three years, and then it stopped and came on only at intervals of from five to six months. Married when twenty-two years of age. When thirty-three years old began to suffer from pain in the chest unaccompanied with cough or respiratory disturbance; the pain afterward extended to shoulder, to half of the neck and head, and the left eye. This continued for about three years, when it completely ceased for a few days and was replaced by a most intolerable vertigo. As this disappeared the pains returned, now associated with feeling of burning in face, swashing sounds in the ear (right), and weakness of memory. Three years later she was troubled with pains in the legs, and now for the first time noticed an enlargement of the face and feet. Two years later she suffered from pains in the hands and forearms, and at one time there was an eruption of pimples on the right forearm. A short time before presenting herself for treatment, after a period of violent pain in the head, she awakened one morning with marked exophthalmos of the left eye and swelling and inflammation of the conjunctiva; this abated, after lasting for fifteen days. With the exception of the absence of prognathism the face is very characteristic; chest is enlarged,

curvature of the spine, no post-sternal dullness, external and internal genitals atrophied, menstruation scanty or absent, continual desire for sexual intercourse, which indulgence is not followed by gratification. The enlargement of the hands and feet is rather typical, except that the hypertrophy seems to be more in the hard than soft parts. The subjective symptoms are still persistent.

OBSERVATION LXXVI.—(Long.) Male, German, aged forty-eight, good family history; denies syphilis; had always been well, except at the age of twenty-five, when, in the German army, he had an abscess on left hip which lasted for five weeks. Came to this country in 1870; married shortly afterward, and from this union were three children, two of whom died in infancy; the third is now a young man and perfectly healthy. Twelve years ago he had an abscess on right hip which was very severe, but he made a good recovery. The symptoms of acromegaly first made their appearance in the hands in 1874; he was then thirty-one years old. Since that time the growth has been constant. Although he is but 5 feet 9½ inches in height, he weighs 262 pounds. The skin is of dirty yellow color. Hands, feet, and face enlarged; cranium normal in size; forehead retreating; hair thick and wiry; nose and lower lip very much enlarged; eyelids and upper lid normal. Marked prognathism; lower jaw greatly hypertrophied; tongue much enlarged; slight cervico-dorsal kyphosis; thyroid gland apparently normal. Hands and arms are typical, the right hand and foot slightly larger than the left. No post-sternal dullness. Genital organs apparently normal; sexual appetite diminished. The thorax, clavicles, and ribs partake of the hypertrophy. Knees and legs enlarged; feet enlarged, flat-footed.

Special senses normal with the exception of sight, which has been lost for ten years, and so completely that he has no perception of light. Eyeballs not greatly pronounced, but marked nystagmus and complete optic atrophy. Patient is of average intelligence, and there is no polyuria, polydipsia or bulimia; measurements given.

OBSERVATION LXXVII.—(Cenas.) A boy, aged fifteen. Mother, who was an alcoholic, died at forty-nine years of age; the patient the youngest of six children and the last child. The mother was drunk at least once a week while carrying this child, and had a tedious labor, lasting five days. Asymmetry of face was noticed at birth. Enlargement of hands and feet, and to some

extent the arms, was remarked when the child was a few months old. The hands and feet continued to enlarge, as the child grew older, out of proportion to the other parts of his body. For past two years he has had frequent fainting-spells of a few minutes' duration. Intelligence less than is common to his age, and frequent headache. The face is round and asymmetrical; hands covered with large violet spots; head large and asymmetrical; feet enormous; forearms small; wrists small; fingers sausage-shape; nails thick and crooked; hands and arms not quite symmetrical; of the right hand all the fingers are affected; of the left, only the thumb and index finger. The legs, thighs, and knees are normal; all the toes of left foot are enlarged, but only the first, second, and fifth of the right are affected. Similar spots on feet as on hands. Head large; marked prognathism of lower jaw; the teeth partake of the enlargement; right side of face larger; and like condition exists in right side of palate, cheeks, lips, and tongue. Thyroid body enlarged on right side. Slight cervico-dorsal kyphosis; no retro-sternal dullness. In lumbar region the skin shows signs of scleroderma. Penis markedly enlarged. Headache, vertigo, and fainting are troublesome. Special senses normal. Voice thick, harsh, and muffled; appetite and thirst increased.

This case has been given somewhat in detail, as it is reported as the only congenital case on record.

OBSERVATION LXXVIII.—(Gerhardt.) Male, aged sixty-two; no family history pertaining to the disease; he has been exposed greatly to inclemency of the weather, and a hard drinker. Has had gonorrhœa and syphilis, intermittent fever, and has suffered severely from bronchial catarrh. Symptoms began in 1888, with pain and swelling in left ankle; then it went to the other ankle, and later to the hands, the right hand being the most severely affected. The pains are intermittent; there is excessive sweating and thirst; the nails are striated and crack easily, and the terminal phalanges are greatly enlarged of the feet and hands.

[It is scarcely possible from the description of this case to see just why it should be classified under acromegaly.]

OBSERVATION LXXIX.—(O'Connor.) Female, born in Ireland, aged fifty, no family history, and with the exception of attacks of headache was healthy during childhood; married at eighteen years of age, and afterward had an

attack of yellow fever. First noticed that she was getting stout in 1883. The hands and feet felt as if bursting, the right hand being first affected, then the left foot. This sensation of fullness was also complained of in the throat. Then the nose began to get red and enlarged, and the voice harsh. The face became enlarged, both transversely and longitudinally lower lip thickened and curled, tongue immense. Hands and feet characteristic. The left foot shows a greater increase than the right, and it has a marked thickened pad beneath metatarsophalangeal region. No enlargement of the bones of the arms or legs. There are distinct circumscribed tumors on some of the bones, such as the seventh rib and the clavicle. The thyroid gland can be made out; she sweats profusely and has great thirst. The menopause occurred at forty-seven years of age.

OBSERVATION LXXX.—(Sommers.) Male, Italian, fifty-one years old; has had large hands and feet since he was twenty years old. They have greatly increased in size in recent years. In 1886 he had a chancre, but no secondary symptoms appeared. In 1870 he had an attack of small-pox. The voice is croaking; he is surly in disposition and very reticent. Forehead narrow, low, and retreating; frontal sinuses large; nose very large; ears immense; lips thick; tongue hypertrophied and deeply fissured; marked prognathism of lower jaw; hands typical in shape, the width and thickness of fingers out of all proportion to the length; palms covered with great pads of tissue, more marked on ulnar side. The enlargement of the feet is of the same character as seen in hands. The great toe is enormous; patellæ are immense; knee-joints crepitate; very slight kyphosis. He weighs 275 pounds, though but 5 feet 11 inches in height. Thyroid small, special senses normal. At the autopsy, the brain and spinal cord was not examined. There was found fatty and cirrhotic liver, enlarged spleen, and absence of thymus.

OBSERVATION LXXXI.—(Bruzzi.) Male, age fifty-one, unmarried, of good family and previous history. No illness of importance in childhood; had spermatorrhœa when a young man. He was of good constitution and development, and performed military service. When twenty-six years of age he had attacks of severe pain in back of head and neck and the dorsal region. At twenty-nine years of age he was impotent, and the pains were troublesome, and he had an attack of nervous prostra-

tion. In 1870 he had an attack of prostration, with delirium and a tendency to coma, in which he remained in an unconscious condition for forty days. His physician diagnosed this as cerebral congestion. After a long convalescence he regained strength, but was troubled with aggravated attacks of dyspepsia. The signs of acromegaly were quite typical, but not of a marked order. Prognathism and kyphosis were not well marked. A full table of measurements appended to original paper.

OBSERVATION LXXXII.—(Gajkiewiczzi.)

OBSERVATION LXXXIII.—(Gause.)

These reports are inaccessible in the time necessary to complete this article. Dercum reported two cases to the American Neurological Association in June, 1892, which have not as yet been published.

Foy has reported a peculiar case, which I have included under this heading for the purpose of drawing attention to local manifestations resembling acromegaly, and to which he has given the name cheiromegaly. The case is in brief as follows: The patient, a refined lady, had had small echondromata removed from her hand twelve months before, and presented herself for the removal of a second such tumor, about the size of a large hen's egg. Shortly after the removal of the second tumor, a strange alteration occurred in the hand; it became broad and large, and very much resembled the hand of acromegaly, but unattended with any other changes or concomitants of acromegaly. The patient died afterward, but from what cause the reporter does not mention.

As yet the most obscure factors concerning acromegaly are the causation and pathology of the disease. As we have already stated in the beginning of this article, its occurrence has been attributed to various factors without its being in any particular instance shown to be dependent upon the attributable causes. Although the majority of the cases have been observed in persons occupying the most lowly walks of life, we cannot say that it is a respecter of persons, for it has been observed in clergymen, officers, and the refined and educated.

Regarding the theories of its pathology, the one looked to with most unanimity is that promulgated by Marie, who is particular to confess that the nature of the disease is wrapped in obscurity, but that the cases which have come to autopsies have shown, with considerable concordance, changes in the pituitary body. Many of the cases still under observation present symptoms, as

can be seen in our abstracts of them, which point with a considerable degree of accuracy to an involvement of this body. In more than one-half the cases reported, eye or ear symptoms, pointing to the pituitary body, have been present and headache in almost every case. What this change in the hypophysis cerebri is, only time and detailed examinations will show. At the same time it is interesting to note instances where the pituitary body has presented changes in conjunction with other diseases without any symptoms of acromegaly developing. Such a case has recently been reported by Wills ("Brain," autumn and winter number, 1892). This patient had pains in the head for fifteen years, which were greatly increased in severity during the last six months. With the exception of progressive dementia, the symptoms were not well marked. There was some paresis of the left internal rectus muscle of the right eye with external strabismus; the other muscles of this eye were normal. Right pupil reacted to light and accommodation, the left to neither; consecutive optic atrophy in both discs. After death a tumor, about the size of a Tangerine orange, divided into two portions, was found wedged in the sella turcica. It lay in the interpeduncular space, extending anteriorly as far as the posterior termination of the orbital surface of the frontal lobes, and laterally it was overhung by the temporo-sphenoidal lobes. Posteriorly it separated the crura cerebri. Anteriorly the olfactory nerves were thin and flattened, the left more than the right, and likewise the optic tracts were more involved on the left side. Microscopical examination showed it to be an adenomata.

Boyce and Beadles have likewise reported three cases in which there was enlargement of the thyroid without symptoms of acromegaly (*Journal of Pathology*, 1892). Two of these cases were of myxœdema and one of sporadic cretinism, and associated with the enlargement of the hypophysis was an atrophied condition of the thyroid glands. Suckling has also seen the same condition in a case of myxœdema.

It has been suggested that in acromegaly the changes in the pituitary and thyroid glands stand in relationship one to the other; that is, when the latter is absent or diminished in size the former is hypertrophied. It has been shown experimentally by Hofmeister (*Fortschritte der Medicin*, No. 4, 1892) and others that after thyroidec-tomy in rabbits the hypophysis increases in weight; but

these experiments have not been corroborated in every instance by other workers in the same line. In acromegaly many of the cases, such as Hudden's, Ballance's, Virchow's, Kanthack's, and others, there was atrophy of the thyroid gland, while in others the gland remained normal or was hypertrophied.

The functions of these two bodies, the thyroid and hypophysis, have yet to be learned; there is no doubt, as has been shown by Rogowitsch, that an intimate connection exists between them and that they stand in a close relationship with the nervous system, particularly the sympathetic. That one should take up the function of the other when diseased is comprehensible even when experiments fail to show that change goes on in the pituitary body after extirpation of the thyroid. The fact that acromegaly does not develop in every case of tumor of the hypophysis cerebri cannot be logically advanced as an argument that its normal existence does not prevent acromegaly; for we know that disease of the spleen is attended with the development of leucocythæmia, yet leucocythæmia does not necessarily follow extirpation of that organ. Nor does myxœdema necessarily accompany disease of the thyroid gland, although in bodies of persons dead from myxœdema, the thyroid is invariably degenerated and generally atrophied.

If acromegaly is dependent on disease of the pituitary body, it does not necessarily follow, as I have before stated (American Neurological Association meeting, June, 1892), that there must be enlargement or tumor of that body. There may be atrophy or parenchymatous degeneration; for if we accept that disease of the pituitary gland has a causative relation to acromegaly, it must be in either one of two ways: Either the pituitary gland—the prehypophysis, so called—secretes and pours out into the circulation certain substances necessary for the preservice of proper nutrition, and the absence of which is manifested by changes in the general system through the nervous system, particularly the sympathetic; or the normal pituitary gland filters out of the blood certain substances the retention of which would give rise to a sort of toxæmia, the consequences of which would be a deleterious action on the nervous system and the resulting changes of the disease. Why there should be a special predilection for the extremities would have to be explained by some conditions of peculiarity of the circulation influenced through the vaso-motors.

It will be seen, from a glance at the literature for the past two years, that the disease known as acromegaly has come to stay, and that a diffusion of knowledge concerning its occurrence is followed by the report of many cases formerly classified under some other heading, but clearly belonging to acromegaly.

Acromegaly is most easily confounded with the disease known as osteo-arthritis hypertrophica pneumique: a disease characterized by enlargement and deformity of the extremities, particularly at the joints, and dependent on some pulmonary disease, most often of a septic nature. It may also be confounded with myxœdema, leontiasis, ostitis deformans of Paget, elephantiasis, erythromelalgia, and rarely, if ever, with arthritis deformans.

In acromegaly the hands are large and thick in appearance, the fingers are uniformly enlarged, and the proportion between the segments of the fingers is well preserved. The nails are flat, small, longitudinally striated, and the flesh has a tendency to grow beyond and around, seemingly imbedding them. In osteo-arthritis of pulmonary origin, the fingers, and not the hand as a whole, are affected. The fingers assume the shape of drum-sticks, and the ends of the bones of the forearm are markedly thickened, projecting voluminously on the dorsal surface of the hand, and the hand, as a whole, shows very evident deformity. The nails become changed, so that they resemble a parrot's beak. This last is a very important factor, and will suggest the diagnosis very quickly; for while, in acromegaly, there is great enlargement, there is no actual deformity, as the relationship between the different parts of the hand is well preserved, and the hypertrophy of the wrist is proportionate to that of the hand in acromegaly. In acromegaly the carpo-metacarpal region is very greatly enlarged, giving rise to the so-called "battle-dore" hand, while in osteo-arthritis this articulation is nearly normal. The same remarks apply to the feet, excepting that there the changes are a little less marked. Another very important difference is that, in acromegaly, the changes are equally in the bones and soft tissues, while in osteo-arthritis the alterations are only in the bones. There are certain parts of the bone—namely, the epiphysis—where a marked predilection exists for these changes.

In acromegaly the face undergoes an important change. There is enormous hypertrophy of the inferior maxilla,

and this gives a characteristic prognathous appearance. In osteo-arthritis the lower jaw is never affected, with the exception of occasional thickening of the alveolar border in both inferior and superior maxillæ. Acromegaly is attended with a more or less well-marked cervico-dorsal kyphosis, which develops early; while such a change, if it occurs at all in osteo-arthritis, is a late manifestation.

In acromegaly there are frequently symptoms referable to the eyes and ears, indicative of change in the pituitary body or adjacent to it; while such symptoms do not exist in osteo-arthritis. Two very constant accompaniments of acromegaly are the development of little nodules of molluscum fibrosum and a large welt of thickened tissue on the inner side of the plantar surface of each foot. These have not been noted in osteo-arthritis.

Finally, osteo-arthritis is always secondary to pulmonary disease, and particularly, as has before been said, pulmonary diseases attended with the production of pus, such as phthisis tuberculosis, empyæmia, pulmonary abscess, and the like.

The decomposition of pus would seem to be the necessary antecedent for the development of the osteo-arthritis, the morbid changes being brought about by the absorption of the products of such decomposition. The *locus* of such purulent change being in the lungs, would seem to facilitate, in some unknown way, the development of the osteo-arthritis. In this disease, likewise, there has been found quite a hereditary element; while in acromegaly, on the other hand, the origin of the disease is in entire obscurity, and, with one possible exception, the disease has shown no hereditary factors in its etiology.

The differential diagnosis from myxœdema is generally not difficult. In myxœdema the face is of a characteristic "full-moon" appearance; the skin is of a peculiar waxy color, with a pinkish tint in cheeks; mentality is sluggish; the chin drops forward on the sternum from sheer inability on the part of the extensors of the head; the skeleton remains free from enlargement. In acromegaly, on the other hand, the outline of the face is elongated; there is marked prognathism; the skin is thickened and muddy-looking; the patient is frequently very alert mentally (Cohen's case); and remarkable changes go on in the skeleton. In myxœdema there is

absence of secretion of sweat and early alopecia; while in acromegaly there is hyperidrosis and thick, tough, wiry hair.

In Paget's disease (osteitis deformans) the bony changes in the upper part of the skeleton are most marked in the cranium. The outer table of the cranial bones becomes porous and spongy, as a result of inflammation, and the normal distinction between the outer table and the inner table and diploë is lost, the entire thickness of the bone consisting of a uniformly compact tissue, in some parts looking like chalk. The bones of the face are but slightly affected, and then only late in the disease; while in the long bones the changes in size and curvature are principally in the shafts, the extremities being scarcely affected. It will be readily seen that these are in marked contrast to the conditions present in acromegaly.

Arthritis deformans, leontiasis, and elephantiasis will scarcely be confounded with acromegaly, if the latter is carefully studied. In leontiasis ossium there is a growth of true bony structures in the shape of tumors of the cranium and face, and generally an absence of hypertrophy of the extremities. In arthritis deformans the changes are confined to the joints of the extremities, the face being rarely affected, and never does it present the elongated face of acromegaly. Elephantiasis consists of cystic and tubular enlargements of the lymphatics—first, of the cutaneous structures, then of the more deeply seated, attended with thickening and induration of the skin and connective-tissue and dilatation and multiplication of the blood-vessels, with wasting of the muscles, and attended with no change in the bony structure. A disease presenting these conditions will scarcely be confounded with acromegaly. Souza-Leite informs us that it is possible to confound acromegaly with the disease to which Weir Mitchell gave the name of erythromelalgia—a word signifying literally pain and redness in a limb. The disease in question is, however, only occasionally attended with an increase in the size of the fingers and hands and a slight fullness of the arms and forearms, and rarely a small degree of kyphosis.

There is, moreover, to assist us in the differential diagnosis, an absence of elongated face and prognathism of the lower jaw, of the enlargement of the lips and tongue, and, in fact, of all the signs referable to the cephalic extremity so apparent and characteristic of

acromegaly. Although enlargement of the extremities may occur in erythromelalgia, it is due to congestion and œdema, and the changes in the fingers, nails, and extremities, so typical in acromegaly, are absent.

Though much new material has been given for observation during the past two or three years, scarcely anything has been added to our knowledge of the causation and nature of the disease and its treatment. Undoubtedly the prognosis in this disease is extremely bad as regards complete recovery, but so few cases have as yet been described from the pathologist's point of view, the disease has not yet been recognized sufficiently long for us to give definite ideas as to its natural duration. It is probably, however, not less than a decade and longer in the greater number of cases. In one case (Bury) the duration of the disease was but three years, while in another (Graham) thirty-four years passed before death occurred. On account of our ignorance of the genesis of the disease, the treatment must be empiric and symptomatic. There has but little been suggested in a therapeutical way since the appearance of Souza-Leite's brochure, in which it is stated that Verstraeten has prescribed in this affection: phosphorus, perchloride of iron, arsenic, rhubarb, etc., and has placed patients on a modified Oertel's regimen, and other plans, but with little promise of success. In a few cases there is an amelioration of some of the symptoms, while other symptoms remain the same or are exaggerated.

Brown has recently stated that his patient was improving under the use of antipyrine and arsenic. Massalonga states that the activity of the disease was held in check by the administration of the salicylates and iodides. For the intense cephalalgia preceding marked manifestations of the disease, and likewise present in the earlier part of the disease, valerianate of caffeine and phenacetine have been found of great service. In cases presenting symptoms of intra-cranial pressure, particularly ocular symptoms, iodide of potash has been given very largely, but without apparent benefit.

The symptomatic treatment consists in combating the headache, overcoming the glycosuria when it exists, and attention to the bulimia, polydipsia, and hyperidrosis, which are frequently troublesome. The glycosuria is generally combated readily by paying attention to the diet and the administration of arsenic and the alkaline waters.

All writers have been impressed with the necessity

of paying attention to the nutrition of the patient from the beginning. The cause of death, in all cases reported as terminating fatally, has been asthenia, from intracranial pressure or from intercurrent acute diseases. The establishment of a high grade of nutrition will prevent these from occurring to some extent, especially the first and the last. Further than this, treatment seems to be of no avail.

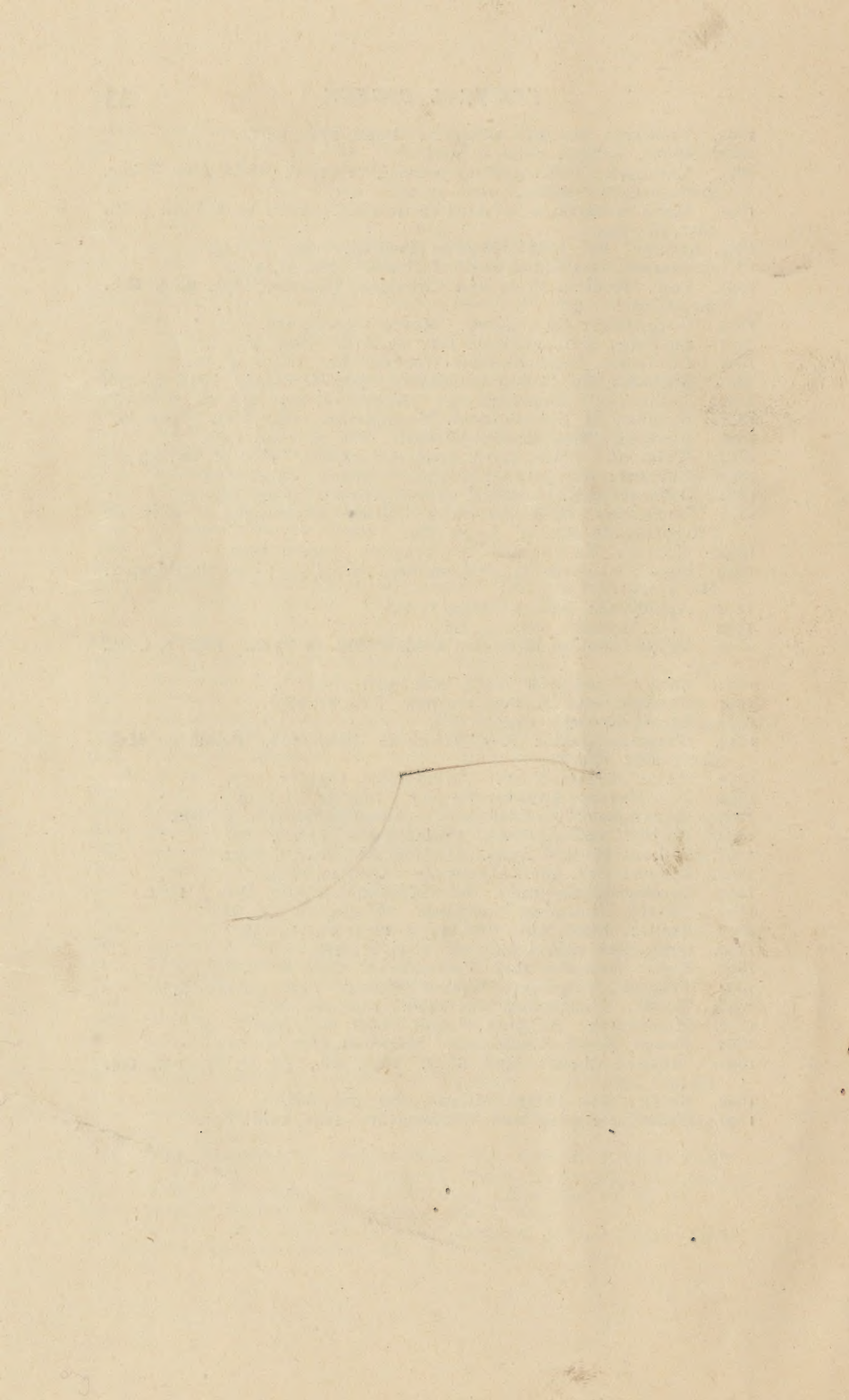
Before closing, it might be well to remark that among English writers there might be a little more unanimity in the spelling of the word which Marie gave to the disease known by his name. There can scarcely be any excuse for writing it, as has been done by a recent writer (Wills), "acromegale;" and the substitution of a *k* for a *c*, in the first syllable, is merely a subserviency to the German, which is unnecessary. The appended bibliography brings the literature of the disease up to the date.

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